ALTERATIONS IN RESPONSE TO SOMATIC PAIN ASSOCIATED WITH ANAESTHESIA

III: THE EFFECT OF HYDROXYDIONE

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In a previous publication, the author reported that an increased sensitivity to pain followed the use of small doses of thiopentone and pentobarbitone (Dundee, 1960), thus confirming the findings of Clutton-Brock (1960). It was suggested that this anti-analgesic action of thiopentone was due to low concentrations of the drug in the brain and the phenomenon was also demonstrated in the postoperative period following moderate and large doses of the drug. On occasions it persisted for as long as five hours after injection of the thiopentone.

Clutton-Brock (1960) has also stated that the anti-analgesic action of the barbiturates is not shared by hydroxydione. This brief communication reports and discusses data which substantiate his findings.

METHOD

The method of study was similar to that used for thiopentone and pentobarbitone and the method of analgesimetry described by Dundee and Moore (1960) was employed. It was not, however, felt justifiable to employ hydroxydione for induction of anaesthesia for dilatation and curettage as in the previous study, although this operation had been found to be particularly suitable for a postoperative study because of the absence of pain. Except where subanaesthetic doses were used all studies were done prior to major abdominal or thoracic surgery no postoperative studies were carried out. All patients received 0.6 mg atropine as sole pre-anaesthetic medication.

RESULTS

Since, in the author's experience, thiopentone is about 2.5 times as potent as hydroxydione as an agent for the induction of anaesthesia, doses of the latter ranging from 2-4 mg/kg were given to 10 patients. In nine of these there was no appreciable alteration in either threshold or response readings during periods ranging from 8 to 10 minutes after injection. The one exception to this is shown in figure 1, which also shows the effect of larger doses of the drug in the period prior to loss of consciousness. The trend was definitely towards a decreased sensitivity to pain and in only one patient could an anti-analgesic action be demonstrated.

![Figure 1](image-url)

The effect of varying single doses of hydroxydione on pain threshold (- - - -) and response (———) readings prior to loss of consciousness. Figures show dosage in mg/kg.
Rises in pain response readings did not occur until three to five minutes after injection, and by this time the narcotic effect of hydroxydione was becoming manifest. It became apparent that the analgesic and narcotic actions of the drug were very closely associated.

The effect of intermittent doses of hydroxydione on pain response readings is shown in figure 2. Here again, the drug produced an appreciable degree of analgesia which was accompanied by a gradual loss of consciousness. This figure also shows the additional analgesia produced by nitrous oxide-oxygen (50 per cent) and the intravenous injection of pethidine. This patient was scheduled for prostatectomy but only a cystoscopy was carried out and so postoperative readings were possible. These failed to detect any anti-analgesic action during the four hours after operation. It is unlikely that these readings were influenced by the small intravenous dose of pethidine.

The occurrence of this greater postoperative comfort is a clinical impression which has not been subjected to detailed study. It may be more apparent than real and depend on the dose of thiopentone used by the anaesthetists who are making this comparison. In a series of major abdominal or thoracic cases, half of whom received 200–300 mg thiopentone (the remainder being given hydroxydione) the author has been unable to detect any less postoperative discomfort or lowered requirements of analgesics with the steroid. With these small doses of thiopentone, the time when the anti-analgesic action would occur was almost certainly passed before the end of the operation.

This discussion is not intended to distract from the value that an intravenous anaesthetic with analgesic properties would have for the anaesthetist. It seems that such a drug will not be a barbiturate. No other intravenous steroid anaesthetics are at present available for clinical study, but it would be of great interest to find whether other similar compounds are devoid of the anti-analgesic action possessed by the barbiturates. If this is the case, then it is hoped that one can be synthesized with the same rapid onset of action as thiopentone.
Because of the close association of analgesia with dulling of consciousness it is unlikely that hydroxydione will have any clinical use as a general analgesic.

**SUMMARY**

Studies show that, unlike the barbiturates, hydroxydione does not increase sensitivity to pain in subanaesthetic doses. There is a gradually increasing analgesia following the injection of anaesthetic doses, but this is paralleled by the hypnotic action of the drug.

It has been suggested that the analgesic action of hydroxydione may be the explanation for the feeling of comfort reported after its use. This feeling of postoperative well-being following hydroxydione may be more apparent than real and depend on the dose of thiopentone given to the series of patients with whom the comparison is made.

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**REFERENCES**


